

Potential anticancer agents identification of *Hystrix brachyura* bezoar through gas chromatography-mass spectrometry-based metabolomics and protein-ligand interaction with molecular docking analyses

ABSTRACT

Background: Bezoar (PB) is a rare, solidified form of undigested food commonly found in the gastrointestinal tract of porcupine (*Hystrix brachyura*). It is believed to be traditionally used to treat various diseases including different kinds of cancers in Malaysia. However, its active principles have not been found out yet. The purpose of this study was to investigate the anticancer property of PB extract as well as to identify the metabolites responsible for its anticancer effect through a widely acclaimed metabolomics approach. Methods: Initially, 25 PB extracts using various solvent ratios of methanol–water (100, 75, 50, 25, 0% v/v) were prepared in regard to metabolomics approach and subsequently the cytotoxicity of each extract was determined against (melanoma) A375 cell line. The metabolites profiling of the most potent extract was conducted using gas chromatography mass spectrometry (GC–MS) and *in silico* investigation was performed on Bcl-2 and cyclin/CDK1 complex protein. Results: The correlation of the bioactivity with GC–MS data produced an orthogonal partial least square (OPLS) model which pinpointed four putative active compounds namely (1) cholest-7-en-3-beta-ol,4,4- dimethyl-,acetate; (2) 4-androsten-4-ol-3,17-dione; (3) isolongifolol and (4) gallic acid. The *in silico* data suggested the binding score and binding mode of active metabolites with the amino acid residues of protein via hydrophobic interactions. Conclusion: This study is the first to report the identified anticancer compounds from PB extract and evaluate them using molecular docking. This further confirms and justifies its traditional usage as an alternative medicine for the treatment of cancer in Malaysia.